The AMPLATZER® PFO Occluder
Instructions for Use
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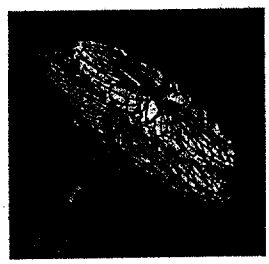

AMPLATZER® Patent Foramen Ovale Occluder System

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician (or properly licensed practitioner).

1. HUMANITARIAN USE DEVICE

Authorized by Federal law for the non-surgical closure of a patent foramen ovale (PFO) in patients with recurrent cryptogenic stroke[1] due to presumed paradoxical embolism through a patent foramen ovale and who have failed conventional drug therapy[2]. The effectiveness of this device for use in this indication has not yet been demonstrated.

2. BRIEF DEVICE DESCRIPTION

The AMPLATZER PFO Occluder is a self-expandable, double disc device made from a Nitinol wire mesh. The two discs are linked together by a short connecting waist allowing free motion of each disc. In order to increase its closing ability, the discs contain thin polyester fabric. The polyester fabric is securely sewn to each disc by a polyester thread.

The AMPLATZER Delivery system consists of a delivery sheath with Touhy-Borst adapter, dilator, loading device, plastic vise and delivery cable. The delivery system was designed specifically to facilitate attachment, loading, delivery and deployment of the AMPLATZER PFO Occluder.

3. INDICATIONS AND USAGE

The AMPLATZER PFO Occluder is indicated for the non-surgical closure of a patent foramen ovale (PFO) in patients with recurrent cryptogenic stroke due to presumed paradoxical embolism through a patent foramen ovale and who have failed conventional drug therapy.

4. CONTRAINDICATIONS

4.1 Presence of thrombus at the intended site of implant, or documented evidence of venous thrombus in the vessels through which access to the defect is gained.
4.2 Active endocarditis or other infections producing bacteremia.
4.3 Patients whose vasculature, through which access to the defect is gained, is inadequate to accommodate the appropriate sheath size.
4.4 Anatomy in which the AMPLATZER PFO device size required would interfere with other intracardiac or intravascular structures, such as valves or pulmonary veins.
4.5 Patients with coagulation disorders who are unable to take antiplatelet or anticoagulant therapy.
4.6 Patients with known hypercoagulable states.
4.7 Patients with intra-cardiac mass or vegetation.

5. WARNINGS

5.1 Patients allergic to nickel may suffer an allergic reaction to this device.

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[1] Cryptogenic stroke – a stroke occurring in the absence of potential phanerogenic cardiac, pulmonary, vascular or neurological sources.
[2] Conventional drug therapy – a therapeutic international normalized ratio (INR) on oral anticoagulants.

5.2 The AMPLATZER PFO Occluder should only be used by those physicians trained in transcatheter defect closure techniques.
5.3 Physicians must be prepared to deal with urgent situations which require removal of embolized devices that result in critical hemodynamic compromise. This includes the availability of an on-site surgeon.
5.4 Embolized devices must be removed as they may disrupt critical cardiac functions. Embolized devices should not be withdrawn through intracardiac structures unless they have been adequately collapsed within the sheath.
5.5 Do not use if the sterile barrier has been compromised in any way.
5.6 Transient hemodynamic compromise may be encountered during device placement, which may require fluid replacement or other medications as determined by the physician.
5.7 Do not release the AMPLATZER PFO Occluder from the delivery cable if the device does not conform to its original configuration or if the device position is unstable. Recapture the device and redeploy. If still unsatisfactory, recapture the device and replace with a new device.
5.8 If the device is in contact with the free atrial wall or any cardiac structures, recapture and replace with a smaller device, if available or abandon the procedure.

6. PRECAUTIONS

6.1 Handling

The AMPLATZER PFO Occluder and Delivery system are for single use only. Do not reuse or resterilize.

6.2 Device Size Selection

- Transesophageal echocardiography (TEE) or similar imaging equipment (i.e., intracardiac echocardiography) is required to measure the distance of the defect to the free atrial wall, atrial septal size and distance to surrounding structures.
- Using the distance of the rim of the defect to the free atrial wall, device selection is as follows:

If the distance from the PFO to the free atrial wall is:	Select:
17.5 mm or greater	9-PFO-035
12.5 to 17.5	9-PFO-025
Less than 12.5 mm	Do not implant device

- See section 9.3 for device sizing method

6.3 Procedural

- Aspirin (3-5 mg/kg/day) (or alternative antiplatelet/anticoagulant if patient has aspirin intolerance) is recommended to be started at least 24 hours prior to the procedure.
- Antibiotics should be administered periprocedurally.
- Patients should be fully heparinized throughout the procedure using adequate dosing so as to keep the ACT greater than 200 msec.

- Transesophageal echocardiography (TEE) or similar imaging equipment (i.e., intracardiac echocardiography) is recommended as an aid in placing the AMPLATZER PFO Occluder. If used, the patient's esophageal anatomy must be adequate for placement and manipulation of the TEE probe.
- Fluoroscopic X-ray guidance is used during placement of the device. The risk of increased x-ray exposure for patients who are pregnant must be weighed against the potential benefits of this technique.
- Do not release the AMPLATZER PFO Occluder from the delivery cable if the device does not conform to the original configuration or if the device position is unstable. Recapture the device and re-deploy. If still unsatisfactory, recapture the device and replace with a new device.
- Care should be taken not to entrap right atrial Chiari networks or large Eustachian valves under the right atrial side of the device.

6.4 Post-Implant

- Patients should take appropriate endocarditis prophylaxis for the 6 months following device implantation. The decision to continue endocarditis prophylaxis beyond 6 months is at the discretion of the physician.
- Patients should be treated with antiplatelet/anticoagulation therapy, such as aspirin for 6 months post implant. The decision to continue antiplatelet/anticoagulation therapy beyond 6 months is at the discretion of the physician.
- The AMPLATZER PFO Occluder is nonferromagnetic. Independent studies of the device in a 1.5 Tesla MRI apparatus detected no magnetic forces.
- If a left-sided thrombus is identified, a patient should be evaluated for a hypercoagulable state and initiation of aggressive anticoagulant therapy should be given. Thrombolysis and surgical removal should be considered if the patient does not respond to anticoagulant therapy.

7. ADVERSE EVENTS

- Potential Adverse Events

Potential adverse events specific to device placement include, but are not limited to: device embolization, thrombus formation on the device surface with the risk of subsequent embolization, and infectious endocarditis.

Placement of the AMPLATZER PFO Occluder involves using standard interventional cardiac catheterization techniques. Adverse events commonly associated with these procedures include, but are not limited to:

Air embolus	Headache/Migraines
Allergic dye reaction	Hematoma and/or pseudoaneurysm
Anesthesia reactions	including blood loss requiring transfusion
Apnea	Hypertension; hypotension
Arrhythmia	Infection including endocarditis
Brachial plexus injury	Perforation of vessel or myocardium
Death	Stroke / Transient Ischemic Attack
Fever	Valvular Regurgitation

- Observed Adverse Events

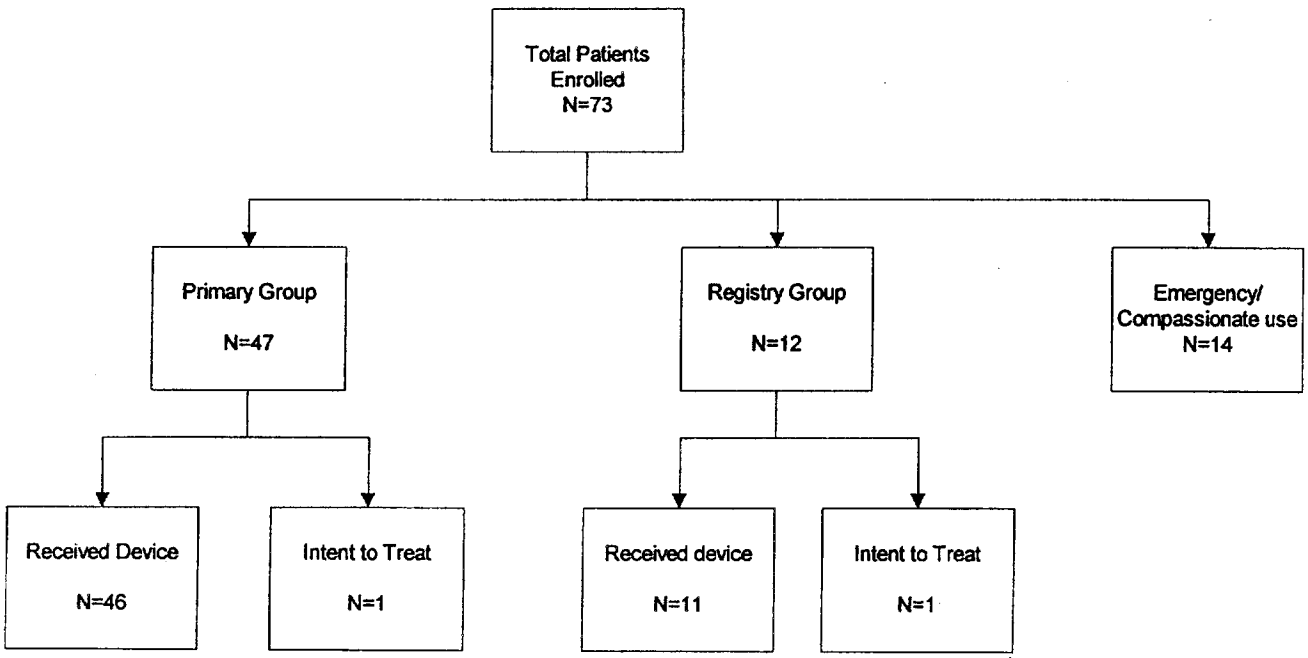
Erosion of the free atrial wall was reported in two patients in international use. Eustachian valve entanglement in delivery system was reported in the literature (1). In the US Phase I study, the following adverse events were determined to be definitely, probably or possibly related to the device or the procedure. Fifteen (15) of the 57 patients who received a device reported 17 adverse events: cardiac arrhythmias (9), chest pain (2), neurologic symptoms (1), hematoma/AV fistula (2), groin pain (1), infection (1), allergic reaction (1).

8. Clinical Experience

a. US Clinical Study

AGA is currently conducting an Investigational Device Exemption (IDE) study to assess the safety and effectiveness of the AMPLATZER PFO Occluder in those patients with a patent foramen ovale (PFO) and history of cryptogenic stroke, TIA and/or peripheral embolization due to presumed paradoxical embolism. The study has a non-randomized pilot phase (Phase I) and a randomized phase (Phase II). Phase I involves 100 patients enrolled at a total of 7 centers.

As of November 15, 2001, there have been 73 patients enrolled in Phase I at 6 investigative sites. Patients were considered enrolled when they signed the informed consent.



1. Primary Group

Table 6. Baseline Demographics- Primary group

Variable		Results
Age (years)	Mean +/- s.d. (N) [range]	41.6+/- 11.2 (47) [14.7,59.1]
Gender		
Female		22/47 (46.8 %)
Male		25/47 (53.2 %)
Height (cm)	Mean +/- s.d. (N) [range]	171.7 +/- 13.0 (47) [130, 195]
Weight (kg)	Mean +/- s.d. (N) [range]	80.2 +/-20.3 (47) [45.0, 118.0]

Table 7 Procedural Information- Primary group

Variable		Results
Heart Catheterization Results:		
Right Atrium Mean	Mean +/- s.d. (N) [range]	6.0+/-3.0 (46) [0.0, 14.0]
Left Atrium Mean	Mean +/- s.d. (N) [range]	8.5 +/-3.8 (38) [2.0, 17.0]
Right Vent. Systolic	Mean +/- s.d. (N) [range]	23.0+/- 6.8 (46) [4.0, 40.0]
Pulm. Artery Systolic	Mean +/- s.d. (N) [range]	21.3+/- 6.9 (44) [7.0, 38.0]
Pulm. Art. Wedge	Mean +/- s.d. (N) [range]	8.9+/- 3.7 (44) [2.0, 17.0]
Size of PFO (mm)	Mean +/- s.d. (N) [range]	5.1+/- 3.8 (24) [1.0, 14.0]
Atrial Septal Aneurysm		15/42(35.7%)
Procedure Time (min.)	Mean +/- s.d. (N) [range]	86.1+/-42.1(43) [21.0, 240.0]
Fluoroscopy time (min.)	Mean +/- s.d. (N) [range]	17.4+/- 15.8 (43) [2.8, 92.0]
Device Size implanted:		
25 mm		22/46 (47.8%)
35 mm		24/46 (52.2%)
Residual Shunt [1]		
Grade 0 (no shunt)		26/46 (56.5 %)
Grade I (minimal shunt)		16/46 (34.8%)
Grade II (moderate shunt)		3/46 (6.5%)
Grade III (severe shunt)		1/46 (2.2%)

Counts may not add up to the number of total patients due to missing data.

[1]Shunt status is calculated based on the maximum amount of crossing bubbles at valsalva release via contrast enhanced echocardiography:

Grad 0- No bubbles Grad I- 1-5 bubbles
Grad II- 6-25 bubbles Grad III- >25 bubbles

Follow up

Twenty-four hours post procedure, a physical exam, EKG, chest X-ray and a 2-D Doppler echocardiogram with contrast at rest and during valsalva maneuver are performed.

Table 8. 24-Hour Follow up- Primary group

Variable	Results
EKG /Holter Monitor EKG Changes	2/32(6.3%)
Chest X-ray results Device position changed	0/44 (0.0%)
Residual Shunt Grade 0 (no shunt) Grade I (minimal shunt) Grade II (moderate shunt) Grade III (severe shunt) Testing not done	 30/44 (68.2 %) 9/44 (20.5 %) 1/44 (2.3 %) 2/44 (4.5 %) 2/44 (4.5%)

Counts may not add up to the number of total patients due to missing data.
[1]Shunt status is calculated based on the maximum amount of crossing bubbles at valsalva release via contrast enhanced echocardiography:

Grad 0- No bubbles Grad I- 1-5 bubbles
Grad II- 6-25 bubbles Grad III- >25 bubble

Table 9. 3-month Follow up-Primary group

Variable	Results
EKG /Holter Monitor EKG Changes	0/26 (0.0 %)
Chest X-ray results Device position changed	0/32 (0.0%)
Residual Shunt[1] Grade 0 (no shunt) Grade I (minimal shunt) Grade II (moderate shunt) Grade III (severe shunt)	 31/34 (91.2%) 3/34 (8.8%) 0/34 (0%) 0/34 (0%)
Closure Success[2]	31/34 (91.2%)

Counts may not add up to the number of total patients due to missing data.
[1]Shunt status is calculated based on the maximum amount of crossing bubbles at valsalva release via contrast enhanced echocardiography:

Grad 0- No bubbles Grad I- 1-5 bubbles
Grad II- 6-25 bubbles Grad III- >25 bubbles

[2]Closure Success is defined as number of patients where the PFO is closed (no bubbles)

2. Registry Group

The registry group consists of patients who have a documented PFO, but have failed conventional drug therapy.

Table 10. Baseline Demographics- Registry group

Variable		Results
Age (years)	Mean +/- s.d. (N) [range]	54.3 +/-19.2 (12) [11.3,81.5]
Gender		
Female		7/12(58.3 %)
Male		5/12(41.7 %)
Height (cm)	Mean +/- s.d. (N) [range]	173.8+/- 13.1 (12) [149.0,190.0]
Weight (kg)	Mean +/- s.d. (N) [range]	78.6+/- 14.3 (12) [47.9,107.0]

Table 11. Procedural Information- Registry group

Variable		Results
Heart Catheterization Results:		
Right Atrium Mean	Mean +/- s.d. (N) [range]	5.4+/-2.9 (12) [1.0,9.0]
Left Atrium Mean	Mean +/- s.d. (N) [range]	5.6+/-3.5 (9) [1.0,9.0]
Right Vent. Systolic	Mean +/- s.d. (N) [range]	24.2+/- 6.1 (12) [9.0,33.0]
Pulm. Artery Systolic	Mean +/- s.d. (N) [range]	21.9+/- 5.4 (12) [10.0,30.0]
Pulm. Art. Wedge	Mean +/- s.d. (N) [range]	8.6+/- 4.5 (11) [1.0,16.0]
Size of PFO (mm)	Mean +/- s.d. (N) [range]	5.1+/- 3.3 (9) [2.0,11.0]
Atrial Septal Aneurysm		3/11 (27.3%)
Procedure Time (min.)	Mean +/- s.d. (N) [range]	68.5+/- 22.0 (12) [43.0,114.0]
Fluoroscopy time (min.)	Mean +/- s.d. (N) [range]	16.2+/- 7.8 (12) [4.4,27.0]
Device Size implanted:		
25 mm		5/11 (45.5 %)
35 mm		6/11 (54.5 %)
Residual Shunt [2]		
Grade 0 (no shunt)		6 /11 (54.5%)
Grade I (minimal shunt)		4/11 (36.4%)
Grade II (moderate shunt)		0/11 (0.0%)
Grade III (severe shunt)		1/11 (9.1%)
Closure Success		6/11 (54.5%)

Counts may not add up to the number of total patients due to missing data.

[1]Shunt status is calculated based on the maximum amount of crossing bubbles at valsalva release via contrast enhanced echocardiography:

Grad 0- No bubbles Grad I- 1-5 bubbles
Grad II- 6-25 bubbles Grad III- >25 bubbles

Follow up

Twenty-four hours post procedure, a physical exam, an EKG, chest X-ray and a 2-D Doppler echocardiogram with contrast at rest and during valsalva maneuver are performed.

Table 12. 24-Hour Follow up- Registry group

Variable	Results
EKG /Holter Monitor EKG Changes	3/9 (33.3%)
Chest X-ray results *Device position changed*	0/11 (0.0%)
Residual Shunt[1] Grade 0 (no shunt) Grade I (minimal shunt) Grade II (moderate shunt) Grade III (severe shunt)	 7/11 (63.6%) 2/11 (18.2%) 0/11 (0.0%) 2/11 (18.2%)

Counts may not add up to the number of total patients due to missing data.
[1]Shunt status is calculated based on the maximum amount of crossing bubbles at valsalva release via contrast enhanced echocardiography:

Grad 0- No bubbles Grad I- 1-5 bubbles
Grad II- 6-25 bubbles Grad III- >25 bubbles

Table 13. 3-month Follow up-Registry group

Variable	N=34
EKG /Holter Monitor EKG Changes	0/6 (100%)
Chest X-ray results Device position changed	0/6 (100%)
Residual Shunt[1] Grade 0 (no shunt) Grade I (minimal shunt) Grade II (moderate shunt) Grade III (severe shunt)	 6/7 (85.7%) 1/7 (14.3%) 0 0
Closure Success[2]	6/7 (85.7%)
Stroke Patients[3] Modified Rankin Scale Score <3 Barthel Index Score <50%	 0/2 (0.0%) 0/2/(0.0%)

Counts may not add up to the number of total patients due to missing data.
[1]Shunt status is calculated based on the maximum amount of crossing bubbles at valsalva release via contrast enhanced echocardiography:

Grad 0- No bubbles Grad I- 1-5 bubbles
Grad II- 6-25 bubbles Grad III- >25 bubbles

[2]Closure Success is defined as number of patients where the PFO is closed (no bubbles)
[3]These indices were done only on patients who suffered stroke.

b. OUS Clinical Experience

The table on the following pages summarizes case histories that have been published, submitted for publication or presented at meetings.

Series	Purpose of Study	# of Patients (P)	Reported Complications Amplatzer PFO Occluder	Observations of study
Windecker, et al[3]	Investigate the long-term risk of recurrent thromboembolic events in patients with PFO and paradoxical embolism after percutaneous PFO closure	80 P attempted; 78 implanted with 5 different devices. **(4 Amplatzer PFO)**	1 device embolization	8 recurrent thromboembolic events (6 TIA's and 2 peripheral emboli) occurred in a mean f-up period of 1.6 ± 1.4 years (range, 0.1 to 5 years)
Windecker, et al[4]	Comparison study to investigate the safety & efficacy of the Amplatzer PFO Occluder.	**29 – Amplatzer (group 1)** 31 - Alternate PFO closure devices (group 2)	0 in group 1 (Amplatzer)	100% successful implant in all patients. Smaller sheath size and shorter fluoro times in group 1; Discharge residual shunt = 4 patients in group 1; 7 patients in group 2. No recurrent thromboembolic events were observed in either group.
Berger F, et al[5]	Report clinical use of the Amplatzer PFO Occluder	73 P; 23 with atrial septal aneurysm	None reported	Successful placement in all P. Mean PFO diameter: 9mm (4-20mm) mean fluoro time 7.5 min (0-23). Complete closure in all patients 12 weeks post procedure.
Berger, et al[6]	To determine if transcatheter closure of PFO prevent renewed cerebral embolic events	185 patients implanted with 5 different devices. **(139 Amplatzer PFO)**	1 report of unexplainable neurological symptoms (unknown which device)	Complete closure in 95.2% of P shown by TEE with contrast during Valsalva 3 months post.
Waight, et al[7]	Report on PFO closure in patients with orthodeoxia-platypnea	4 patients **(2 Amplatzer PFO)**	None reported	Average saturation increased from 81% to 96% with complete resolution of symptoms
Wahl, et al[8]	Assess long-term risk and risk factors for recurrent embolism after perc PFO closure	152 attempts with 6 different type devices **(45 Amplatzer PFO)**	0 procedural complication; 0 recurrent embolism 3 residual shunts	150 P received devices; 6 yr F-up (1.7 ±1.6 yrs; 258 P yrs) 1 recurrent stroke; 6 TIAs and 2 peripheral emboli

[3] Windecker S, Wahl A, Chatterjee T, et al: Percutaneous Closure of Patent Foramen Ovale in Patients with Paradoxical Embolism – Long-Term Risk of Recurrent Thromboembolic Events. *Circulation*, 2000;101:893-898

[4] Windecker S, Wahl A, Becker U, et al: Percutaneous closure of Patent Foramen Ovale in Patients with paradoxical Embolism using the Amplatzer PFO Occluder. *Submitted for publication*

[5] Berger F, Ewert P, Dahnert I, et al: Experience with the new amplatzer PFO occluder for occlusion of patent foramen ovale (PFO) after presumed paradoxical embolism. *Cardiol Young:* Vol 10, Supp 2; XXXV Annual General Meeting of the AEPC. P159.

[6] Berger F, Ewert P, Dahnert I, et al: Up to 8 years follow-up after interventional closure of patent foramen ovale (PFO) as a prevention of paradoxical embolism. *Cardiol Young:* Vol 10, Supp 2; XXXV Annual General Meeting of the AEPC. P134

[7] Waight DJ, Cao QL, and Hijazi AM: Closure of patent foramen ovale in patients with orthodeoxia-platypnea using the amplatzer devices. Catheter Cardiovasc Interv. 2000 Jun;50(2):195-8.

[8] Wahl A, Meier B, Haxel B, et al: Prognosis after percutaneous Closure of Patent Foramen Ovale in Patients with Paradoxic Embolism. *Neurology* 2001;57:1330-1332

Series	Purpose of Study	# of Patients (P)	Reported Complications Amplatzer PFO Occluder	Observations of study
Demkow, et al[9]	Report initial experience of Amplatzer PFO device in Poland.	3 P with at least one ischemic stroke episode	None	Complete closure confirmed at one month follow-up echocardiogram in each P. No repeat cerebral accidents reported.
Beitzke, et al[10]	Report experience with catheter closure of PFO using 4 different devices between June 1995 and June 2000.	162 P **(59 Amplatzer PFO)**	1 Arrhythmia	Implantations successful in all P. Serious catheter-related complications include 2 device embolizations and 2 venous bleedings. Residual leaks were reported in 5/116 patients with one receiving a second device for closure. Follow-up of 19.4 ± 16.2 months per patient, TIA and PRIND occurred in 3/116 P.
Sievert, et al[11]	Report experience with catheter closure of PFO using 7 different devices since August 1994.	281 P **(57 Amplatzer PFO)**	None	Implantations successful in all P. F-up of 1 – 71 months, recurrent embolic event occurred in 8 P (not with Amplatzer)
Beitzke, et al[12],	Report experience with catheter closure of PFO using 5 different devices between June 1995 and November 2000	202 P **(82 Amplatzer PFO)**	UNK	Early complications included 2 device embolizations, 5 retroperitoneal hematomas and 2 cardiac perforations; 8 late arrhythmias; 3 TIA following procedure. 175 patients followed for 3 to 62 months. 170 patients with 204 symptom-free patient years.
Krumsdorf U, et al[13]	Analyze morphological and functional characteristics of atrial septal aneurysm in PFO and ASD patients and to assess the feasibility and efficacy of 7 different devices between March 1997 and May 2000.	51 P **(5 Amplatzer PFO)**	None	Implantations successful in all patients. During follow-up, (0.6 – 37 months), a residual shunt was observed in 4 P 2 weeks after implantation and in 1P 6 months after implantation.
Schwerzmann M, et al[14]	Compare the incidence of procedural complications and residual shunt between the Amplatzer PFO Occluder and another PFO device.	121 P **(66 Amplatzer PFO)**	There were more minor and major adverse events with the other PFO device than with the Amplatzer device (14.6% vs. 1.5%).	More attempts were required for placing the other device (9.1% vs 1.5%); larger sheath size required for the other device and significant residual shunt 6 months after closure persisted more frequently in the other device.

[9] Demkow M, Ruzytto W, Kwiecinski H, et al: Transcatheter closure of patent foramen ovale after cryptogenic stroke. Neur Neurochir Pol 2000 T.34(L), NR5 1005-1014

[10] Beitzke A, Schuchlenz H, Gamillscheg A, et al: Catheter closure of the persistent foramen Ovale: Mid-Term Results in 162 Patients. *J Interven Cardiol* 2001;14:223-230

[11] Sievert H, Horvath K, Zadan E, et al: Patent Foramen Ovale Closure in Patients with Transient Ischemia Attack/Stroke. *J Interven Cardiol* 2001;14:261-266.

[12] Beitzke A: PFO Closure: has its time come too? 3rd World Congress of Pediatric Cardiology, 2001. P834

[13] Krumsdorf U, Keppeler P, Horvath K, et al: Catheter Closure of Atrial Septal Defects and Patent Foramen Ovale in Patients with an Atrial Septal Aneurysm Using Different Devices. *J Interven Cardiol* 2001:14:49-55

Series	Purpose of Study	# of Patients (P)	Reported Complications – Amplatzer PFO Occluder	Observations of study
Spadoni I, et al[15]	Report experience of transcatheter PFO closure	39 P **(11 Amplatzer PFO)**	None	No recurrences of thromboembolic events in 30 P with paradoxical embolism.
Trepels T, et al[16]	Report first known case of penetration of an Amplatzer PFO occluder	71 P in series	One patient experienced pericardial tamponade	Surgery to remove the device revealed erosion of the right atrial roof and the aortic root.
Onorato E, et al[17]	Verify the role of ICE in transcatheter closure of PFO	103 P	None	No residual shunt and no recurrent symptoms 12 months post implant.
Anzola GP, et al[18]	Monitor the passage of microembolic signals in brain vessels	29 P	None	Complete occlusion in 28/29 P after 1 month. Severity of migraine dropped from a mean of 6 to a mean of 3 post closure.
Onorato E, et al[19]	Report combined use of ICE and TCD to quantify right to left shunts in real time.	31 P **(29 Amplatzer PFO)**	None	Mean fluoroscopy and procedural times were 9.45 $\pm$ 5 minutes and 57 $\pm$ 21 minutes, respectively.
Onorato E, et al[20]	Report on a patient with PFO with ASA and prominent Eustachian valve who underwent transcatheter closure	1	Prominent valve tissue was entrapped on the delivery cable and a piece of the EV was extracted unintentionally.	TTE 3 and 12 months post confirmed an ideally positioned device with no interference by the EV and no residual shunt.
Sievert, et al[21]	Report recurrent embolic TIA and stroke rate of patient implanted with closure devices	250 P **(44 Amplatzer PFO)**	Unknown	Annual event rate after PFO closure was 2.1%. Catheter closure of PFO reduces but does not eliminate the risk of cerebral events. During 235 patient-years, 5 P suffered from a recurrent embolic event (1 minor stroke, 4 TIA's). Unknown which device(s)

[14] Schwerzmann M, Meier B, Wahl A, et al: Percutaneous closure of patent foramen ovale in patients with paradoxical embolism: Impact of PFO dedicated devices on procedural complications and residual shunt. *4th International Workshop Catheter Interventions in Congenital Heart Disease*. October 18-20, 2001, P536

[15] Spadoni I, Giusti S, Carminati M, et al: Indications and results of transcatheter closure of patent foramen ovale (PFO). *4th International Workshop Catheter Interventions in Congenital Heart Disease*. October 18-20, 2001, abstract

[16] Trepels T, Sievert H, Billinger K, et al: Amplatzer-PFO-occluder: Case report of a perforation. *4th International Workshop Catheter Interventions in Congenital Heart Disease*. October 18-20, 2001, abstract

[17] Onorato E, Pera I, Melzi G, et al: Intracardiac echocardiography: a novel approach to patent foramen ovale transcatheter closure. *4th International Workshop Catheter Interventions in Congenital Heart Disease*. October 18-20, 2001, abstract

[18] Anzola GP, Angeli S, Morandi E, et al: Transcranial doppler monitoring of right-to-left shunt during transcatheter closure of PFO: clues for migraine treatment? *4th International Workshop Catheter Interventions in Congenital Heart Disease*. October 18-20, 2001, abstract

[19] Onorato E, Pera I, Melzi G, et al: Intracardiac Echocardiography and transcranial doppler ultrasound to guide transcatheter closure of PFO. *4th International Workshop Catheter Interventions in Congenital Heart Disease*. October 18-20, 2001, abstract

[20] Onorato E, Pera I, Melzi G, et al: Large redundant eustachian valve interfering with Amplatzer PFO occluder placement: anatomo-clinical and technical implications. *4th International Workshop Catheter Interventions in Congenital Heart Disease*. October 18-20, 2001, abstract

Series	Purpose of Study	# of Patients (P)	Reported Complications Amplatzer PFO Occluder	Observations of Study
Butera, et al[22]	Report recurrent thromboembolic event rate using 4 different devices.	35 **(3 Amplatzer PFO)**	None	No residual shunt at 1 month follow-up. No patient experienced recurrence of a thromboembolic event.
La Rosee, et al[23]	Report results of one centers experience with different occlusion systems	102 **(UNK # Amplatzer PFO)**	Unknown	Successful placement in 99 of 102 patients. Occluder associated problems were: mild (41%) or extensive (11%) thrombus formation on the device; minor displacement (10%) or broken umbrella strut (6%). One patient experienced percardial tamponade which requried emergency surgical intervention. Complete occlusion was achieved in 71%. No case of cerebral emboli.
Pinto, et al[24]	Report on first three cases using the AMPLATZER PFO Occluder in Portugal	3	None	Procedure time ranged from 30-55 minutes and fluoro time 9-12 minutes. During the short follow-up all patients are asymptomatic and free of recurrent events.

[21] Sievert H, Horvath K, Zadan E, et al: Catheter Closure of PFO reduces but does not eliminate the risk of cerebral events: Acute and follow-up results in 250 patients. TCT Abstracts/ Poster, October 19, 2000; abstract number TCT-157.

[22] Butera G, Bini MR, Chessa M, et al: Transcatheter closure of patient foramen ovale in patients with cryptogenic stroke. *Ital Heart J* 2001 Feb;2(2): 119-20

[23] La Rosee K, Krause D, Becker M, et al: Transcatheter closure of atrial septal defects in adults. Practicality and safety of four different closure systems used in 102 patients. *Dtsch Med Wochenschr* 2001 Sep 21;126(38):1030-6

[24] Pinto FF, Sousa L, Abreu J, et al: Percutaneous occlusion of Patent Foramen Ovale in Patients with Paradoxical Embolism. *Rev Port Cardiol* 2001;20(7-8):747-757.

9. DIRECTIONS FOR USE

9.1 Maintaining Device Effectiveness

- Do not attempt to use the device or delivery system after the Expiration Date noted on the label.
- Storage is recommended in a cool, dry place.
- Do not attempt to repair or reuse damaged product. Do not reuse or resterilize product. Return to AGA Medical for replacement.

9.2 Complete Device Description

The AMPLATZER PFO Occluder and AMPLATZER Delivery System are packaged separately. Both components are sterilized via ETO.

9.2.1 AMPLATZER PFO Occluder

The AMPLATZER PFO Occluder is a self-expandable, double disc device made from a Nitinol wire mesh. The two discs are linked together by a short connecting waist allowing free motion of each disc. In order to increase its closing ability, the discs contain polyester fabric. The polyester fabric is securely sewn to each disc by a polyester thread.

Platinum marker bands are applied to the wire ends and laser welded. The braiding is then formed via heat-treatment. After cooling, a stainless steel sleeve with a female thread is welded to the marker band using advanced laser technology.

Order Number	Right Atrial Disc Diameter	Left Atrial Disc Diameter
9-PFO-025	25mm	18mm
9-PFO-035	35mm	25mm

9.2.2 AMPLATZER Delivery System

The AMPLATZER® Delivery System includes:

- **Delivery Sheath with Touhy-Borst Adapter** - used to deliver the device.
- **Dilator** – used to ease penetration of tissue.
- **Loading Device** – used to introduce the AMPLATZER PFO Occluder into the delivery sheath.

- **Plastic Vise** – facilitates direction control and serves as the "handle" for disconnecting (unscrewing) the delivery cable from the device.
- **Delivery Cable** – the device is screwed onto the distal tip of the delivery cable, which allows for placement (and if necessary, retrieval) of the device.

9.3 Device Selection

- Using Four Chamber view, measure the distance from the rim of the defect to the rim of the superior atrial wall (Figure 1, #2).
- Using TEE Short Axis view, measure the distance from the rim of the defect to the aortic mound (anterior superior rim) (Figure 2, #7).

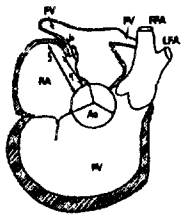


Figure 1
Four Chamber View

1. Total Septal Length measured at maximal atrial dimension.
2. **Superior vena cava to the edge of the defect**
3. Pulmonary vein to edge of defect
4. Edge of defect to mitral valve

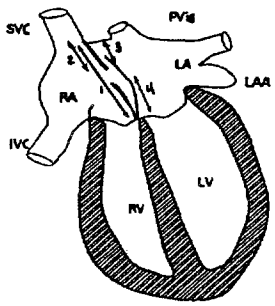


Figure 2
TEE Short Axis View

5. Posterior rim length.
6. Posterior rim to the edge of the defect.
7. **The distance from the edge of the defect to the aortic mound (which is the Anterior Superior Rim). If the septal primum and limbus fossae ovalis form a tunnel, measure the distance from the right atrial aspect of the tunnel to the aortic mound.**

Measurement 6 and 7	Select:
If both are: 17.5 mm or greater	9-PFO-035
If either are: 12.5 to 17.5	9-PFO-025
If either are: Less than 12.5 mm	Do not implant device

WARNING: Do not implant a device is the distance from the PFO to the free atrial wall is less than 12.5 mm (as measured by echo).

9.4 Directions for use

- Patients should be fully heparinized throughout the procedure using adequate dosing so as to keep the ACT greater than 200 msec.

- Following percutaneous puncture of the femoral vein, perform a standard right heart catheterization. Pass a diagnostic catheter through the PFO into the left atrium and introduce an exchange "J" guidewire (2 cm tip) into the left atrium.

- Using transesophageal echocardiography (TEE) or similar imaging equipment (i.e, intracardiac echocardiography), measure the distance of the defect to the free atrial wall, atrial septal size and distance to surrounding structures (reference 8.3 for device selection).

- Pass the delivery cable through the loader and screw the device on to the delivery cable.

- Once the device is securely attached to the cable, immerse the device and loader in saline solution and pull the device into the loader.

- Remove the catheter leaving the guidewire in place.

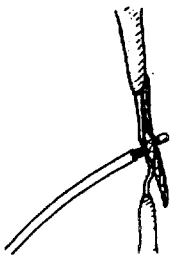
- Insert the dilator into the delivery sheath and secure to the sheath with the locking mechanism. Introduce the dilator/delivery sheath assembly. Once the delivery sheath has reached the inferior vena cava, remove the dilator to allow back bleeding to purge all air from the system.

- Connect the hemostasis valve and flush with a syringe before the left atrium is entered.

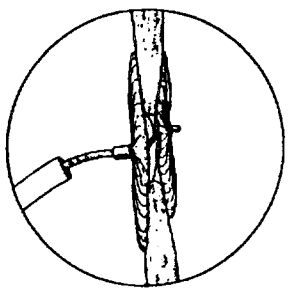
- Advance the sheath over the guidewire through the PFO and into the left atrium. Correct position of the delivery sheath is verified by a test injection of contrast medium. Once in satisfactory position, remove the guidewire and flush the sheath with saline.

- Introduce the loading device to the delivery sheath. Advance the device into the sheath by pushing (not rotating) the delivery cable.

- Under fluoroscopic and echocardiographic guidance, deploy the left atrial disc by pulling firmly against the atrial septum, which can be felt and observed via ultrasonography.



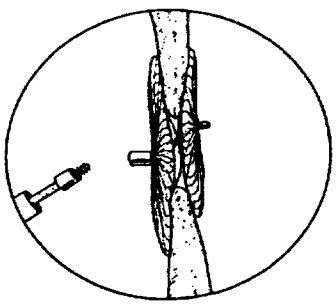
- With gentle tension on the delivery cable, pull the sheath back to deploy the right atrial disc. To and fro motion with the delivery cable assures secure position across the patent foramen ovale, which can be observed by ultrasound and fluoroscopy.



- Confirm correct placement. Advance the sheath close to the right atrial disc and administer an injection of contrast medium to confirm correct position.

WARNING: **Careful assessment of the edge of the device along the free atrial wall by echocardiography and angiography must be completed. If the device is in contact with the free atrial wall, the device must be removed and replaced with a smaller device, if available or the procedure abandoned.**

- Release the device. Attach the plastic vise to the delivery cable, tighten the screw and unscrew the device from the cable by turning the cable counterclockwise (indicated by the arrow on the vise). In the unlikely event that this should not be possible, the sheath can be advanced against the right atrial disc to fix the device which facilitates detachment.



WARNING: **Do not release the AMPLATZER PFO Occluder from the delivery cable if the device does not conform to its original configuration or if the device position is unstable. Recapture the device and redeploy. If still unsatisfactory, recapture the device and replace with a new device.**

9. USE IN SPECIFIC POPULATIONS

- **Pregnancy** – care should be taken to minimize the radiation exposure to the fetus and the mother.
- **Nursing Mothers** – There has been no quantitative assessment of the presence of leachables in breast milk.

10. POST PROCEDURE PATIENT REGISTRATION / INFORMATION

- ***Peel Off Labels*** *- Peel Off labels are provided for the patient's chart and for the patient registration card. These labels specify the size, lot and serial number of the device.*

- **Patient Registration Card** - A Patient Registration Card is located in each device box. Complete the patient information section and send the card to AGA Medical Corporation.

- **Patient Identification Card** - Complete the information on the temporary Patient Identification Card and give to the patient before they leave the hospital. Upon receipt of the Patient Registration Card, AGA Medical will generate a permanent ID card and send directly to the patient.